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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/035,100	12/28/2001	Erik Ho Fong Wong	00378.US1	1691

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EXAMINER	
SPIVACK, PHYLLIS G	
ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 06/27/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/035,100	Wong et al.
Examiner	**Art Unit**
Phyllis G. Spivack	1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 9, 2003* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-22* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Applicants' Election of Species pursuant to 37 C FR 1.143 filed April 9, 2003, Paper No. 5, is acknowledged. Applicants have elected reboxetine as the norepinephrine reuptake inhibitor and clozapine as the neuroleptic agent.

Claims 1-22 are presented and represent all of the claims under consideration.

The disclosure is objected to for the following informality:

Claims 1 and 22 are seen as substantial duplicates. Intended use confers no patentable weight to composition claims. **In re Hack** 114 USPQ 161.

Appropriate correction is required.

Claims 1-22 are rejected under judicially created doctrine as being drawn to an improper Markush group. Lack of unity of invention has been found to exist since a common nucleus among the various norepinephrine reuptake inhibitors, and also, among the various neuroleptic agents, is absent. A prior art reference anticipating the claims under 35 U.S.C. 102 with respect to one combination composition, as, for example, venlafaxine and chlorpromazine, would not render the same claim obvious under 35 U.S.C. 103 with respect to another combination composition, such as reboxetine and clozapine.

As Markush claims that lack unity of invention, claims 1-22 will be examined fully only with respect to the elected species and further to the extent necessary to determine patentability. MPEP 803.02.

Claims 9-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the

art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are directed to the treatment of any disease or disorder of the central nervous system. The specification provides support for the treatment of schizophrenia comprising administering the norepinephrine reuptake inhibitor reboxetine in combination with a neuroleptic which is clozapine, olanzapine or risperidone.

Attention is directed to In re Wands, 8 USPQ2d 1400 where the court set forth factors to consider when assessing whether or not a disclosure would require undue experimentation. These factors are:

1) the quantity of experimentation necessary

2) the amount of direction or guidance provided

3) the presence or absence of working examples

4) the nature of the invention

5) the state of the art

6) the relative skill of those in the art

7) the predictability of the art and

8) the breadth of the claims.

The instant specification fails to provide guidance that would allow the skilled artisan background sufficient to practice the instant invention without resorting to undue experimentation in view of further discussion below.

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

The claimed invention relates to treatment of any disease or disorder of the central nervous system.

The relative skill of those in the art is generally that of a Ph.D or M.D.

Each particular neurologic disease or disorder has its own specific characteristics and etiology. The unpredictability observed with single agent therapy is compounded when a combination of agents is employed. The broad recitation "treating a disease or disorder of the central nervous system" in inclusive of many conditions that presently have no established successful therapies.

It is clear the art to which the present invention relates is highly unpredictable and unreliable with respect to conclusions drawn from laboratory data extrapolated to clinical efficacy.

The breadth of the claims

The claims are very broad and inclusive of any disease and disorder of the central nervous system.

The amount of direction or guidance provided and the presence or absence of working examples

The working examples are limited to the combination of reboxetine and clozapine, olanzapine or risperidone for treatment of schizophrenia.

The quantity of experimentation necessary

Applicants have failed to provide guidance as to which particular norepinephrine reuptake inhibitor in combination with which particular neuroleptic would be preferred for treatment of the many other diseases or disorders of the central nervous system, besides schizophrenia, that are recited in claim 10. The skilled artisan would expect the interaction of a particular combination of drugs in the treatment of a particular disease state to be very specific and highly unpredictable absent a clear understanding of the structural and biochemical basis for each agent. The instant specification sets forth no such understanding nor any criteria for extrapolating beyond the combination of reboxetine and clozapine, olanzapine or risperidone. Even for the combinations set forth, no direction is provided to treat any other condition beyond schizophrenia. Absent reasonable *a priori* expectation of success for using a particular chemotherapeutic combination to treat any particular CNS disease, one skilled in the neurology art would have to test extensively many combinations of agents to discover which particular CNS respond to that particular combination. Since each prospective embodiment, as well as future embodiments as the art progresses, would have to be empirically tested, undue experimentation would be required to practice the invention as it is claimed in its current scope. The specification provides inadequate guidance to do otherwise.

Claims 19-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 19-21 provide for the use of a composition, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 19-21 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

The elected species appears to be free of the prior art. Accordingly, the search has been extended according to current Markush practice.

Claims 1-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koch et al., Eur. J. Clin. Pharmacol. (abstract).

Koch teaches the administration of the norepinephrine reuptake inhibitor reboxetine with the neuroleptic agent olanzapine in the treatment of the central nervous system disease schizophrenia. The claims differ in that Koch discloses a polypragmatic treatment for schizophrenia wherein multiple drugs, in addition to the norepinephrine reuptake inhibitor and the neuroleptic, are simultaneously administered. One skilled in the art would have been motivated to administer various agents in the treatment of schizophrenia in view of Koch's teaching. Such would have been obvious in the absence of evidence to the contrary because depression,

fluctuations in mood and cognitive impairment are some of the multiple parameters in the disease process that require chemotherapeutic consideration. The determination of an optimal optical isomer of reboxetine, modes of administration, dosages, dosing regimens and a delivery vehicle are parameters well within the purview of those skilled in the art through no more than routine experimentation.

No claim is allowed.

Any inquiry concerning this communication should be directed to Phyllis Spivack at telephone number 703-308-4703.

June 26, 2003

Phyllis Spivack

PHYLLIS SPIVACK
PRIMARY EXAMINER